The following table lists the top 10 drugs by total dollars paid. While these medications collectively accounted for 27.6% of the program's total drug expenses, they accounted for only 10.4% of all prescriptions. The average amount paid per prescription ($138.68) was also significantly more than the average amount paid per prescription for all drugs ($52.03). Eight of the top ten drugs are within the CNS agent therapeutic class.

Top 10 Drugs Base on Amount Paid*

Drug	Therapeutic Class	Paid	Rx	Paid/Rx	% of Total Program Expense
Olanzapine (Zyprexa)	Antipsychotics	$14,673,025	53,161	$276.01	6.30%
Risperidone products (Risperdal)	Antipsychotics	$10,303,472	65,380	$157.59	4.40%
Quetiapine (Seroquel)	Antipsychotics	$8,190,956	47,295	$173.19	3.50%
Lansoprazole (Prevacid)	Anti-ulcer	$6,371,994	51,941	$122.68	2.70%
Divalproex (Depakote)	Anticonvulsants	$5,421,895	56,605	$95.78	2.30%
Gabapentin (Neurontin)	Anticonvulsants	$5,104,437	45,980	$111.01	2.20%
Sertraline (Zoloft)	Antidepressants	$4,671,788	64,323	$72.63	2.00%
Celecoxib (Celebrex)	Analgesics	$3,317,730	36,621	$90.60	1.40%
Oxycodone (Oxycontin)	Analgesics	$3,137,206	17,717	$177.07	1.40%
Omeprazole (Prilosec)	Anti-ulcer	$3,008,527	23,915	$125.80	1.30%
TOTAL TOP 10		$64,201,031	462,938	$138.68	27.60%

***Reflects cost per ingredient plus dispensing fee and before manufacturer rebates**

Mirtazapine, a tetracyclic agent, is a relatively new antidepressant. It differs structurally from the SSRIs, monoamine oxidase inhibitors, and tricyclic antidepressant agents. It exerts antagonistic activity at central alpha$_2$ receptors and both the 5HT$_2$ and 5HT$_3$ receptors and is sometimes referred to as a noradrenergic and specific serotonergic antidepressant. Mirtazapine *exhibits anxiolytic and sedative effects,* probably secondary to the 5HT$_2$ receptor blockade activity. Some studies suggest that mirtazapine demonstrates an earlier onset of action than the SSRIs in patients with major depressive disorder.[1] It exhibits moderate peripheral α_1-adrenergic blocking activity that may explain the occasional orthostatic hypotension that reportedly has been associated with mirtazapine.[2] The drug is also a moderate antagonist at muscarinic receptors, which may account for the relatively low incidence of anticholinergic effects.[2] During the most recent program assessment period for Kansas, mirtazapine accounted for 9% of the submitted prescriptions within the antidepressant class and nearly 11.2% of the antidepressant program expense.[3] The recommended dosage range is 15-45 mg daily as a single dose at bedtime. While mirtazapine is available as the brand Remeron®, it is now available in a generic formulation and represents a cost savings ranging from $9 – $17 per Rx depending on the dosage prescribed.

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We welcome the opportunity to discuss with you any comments or concerns you may have about this Newsletter. Please call our office at 1-800-745-1946 with any questions or concerns.

Heritage Information Systems, Inc.

Kansas Medical Assistance Program

Drug Utilization Review Bulletin

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Are SSRIs the Same for First-Line Treatment of Depression?

By Ellen Friedla, Pharm D, BCPS, MPH

Depression is an international public health issue[1] with impairments in social and occupational functioning, increased comorbidity of psychiatric and medical conditions, and an increased risk of mortality among depressed individuals as a few of its consequences.[2] Moreover, depression-related morbidity comes at a price to society -- the economic impact of depression on the US economy has been estimated at more than tens of billions of dollars per year.[3]

The development of the five selective serotonin reuptake inhibitors (SSRIs) in the past decade and a half has greatly enhanced the treatment of depression by offering patients medications that are as efficacious as the older agents but are generally more tolerable and safer in an overdose.[4,5]

In general, the SSRIs (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline) are used as first-line treatment for adult depression in the primary care setting[6,13] and have become the most commonly prescribed class of antidepressants, accounting for $13.2 million of the annual prescription expenditure and nearly 5.4% of the total drug expenditure within the Kansas Medical Assistance Program.[7] According to recent data, the physician prescribing patterns indicate SSRI dispensing growth at a rate of 25% each year.[11]

Although each SSRI has demonstrated effectiveness, there is no comparative randomized trial data supporting the superiority of one SSRI relative to another.[6,8,9] When patients are maintained on the SSRI antidepressant for the first 180 days of therapy, achieving the minimum duration of therapy to prevent acute depression episodes and relapse, the SSRIs do not differ across a wide array of psychological, social, work, or other health-related quality of life outcome domains in either magnitude or time course of response at 3-months and 9-months using the Medical Outcomes Summary scoring.[10,11] Previous prospective studies, comparing two antidepressants in psychiatric inpatients, have shown that SSRIs are equally efficacious with one another as well as with the newer SSRIs antidepressants in alleviating depressive symptoms.[6,8] Some comparative and retrospective studies evaluating the effectiveness and clinical outcomes of SSRI antidepressants reported differences, although these studies had short follow-up periods, a limited range of outcomes measured, and predominantly recruited participants from psychiatric inpatient settings.[10] Since most patients with depression are treated in the primary care setting, it is important to compare studies which were performed in an outpatient setting to reflect the real clinical venue.

In retrospective studies, citalopram, fluoxetine, sertraline, and paroxetine were associated with similar incidence of clinically significant adverse effects and rates of discontinuation or switching.[10-11] Interestingly, the drug safety profile data for these agents are significant since discontinuation or switching to another agent generally represent an adverse event severe enough to prompt a change and typically result in increased drug therapy costs (switching to another SSRI or another antidepressant drug class). However, escitalopram, the newest SSRI launched in late 2002, has several comparative drug safety analysis studies with the other SSRI antidepressants underway.[14]

Retrospective studies suggest the emergence of bothersome symptoms does not differ within the SSRI antidepressant drug class[9,12]. The occurrence of severe adverse events was rare and included the following: bowel complaints (2.0%), stomach pain (1.5%), nausea or dyspepsia (1.3%), insomnia (1.3%), dizziness (1.1%), and headache (0.4%).[10-12] Two retrospective review studies suggest comparable discontinuation rates of fluoxetine, paroxetine, sertraline, and citalopram ranging from 10 to 12 % over a 6-month period.[11,13] This trend is important since early discontinuation of antidepressant treatment has been associated with increased medical costs. As discussed earlier, SSRI antidepressants have similar efficacy, adverse events profiles, switching, and discontinuation rates in adults. These variables are important to consider when making economic comparisons between agents, as the SSRI selected can have an impact on the overall costs of drug therapy.

The treatment of depression has improved with the advent of the SSRI agents.

(continued on next page)

SSRIs cont.

These agents are comparably efficacious to the older antidepressants but are considerably more tolerable. Varying costs of SSRI antidepressants can have important implications for health care costs (see Table 1 for SSRI Antidepressant Cost Comparison). Although there may be some characteristics of any medication that distinguish its use in an individual patient, our review of clinical findings suggest that in general none of the SSRIs currently available can be recommended over another in terms of effectiveness. Fluoxetine offers favorable pricing and may be the agent of choice in the SSRI naïve patient.

Table 1: SSRI Antidepressant Cost Comparison

Drug	Usual Dosage Per Day*	AWP Per Month ($)†
Fluoxetine‡	20mg – 80mg	18 - 241§
Lexapro®	10mg – 20mg	69 - 72
Celexa®	20mg - 40mg	75
Paroxetine	20mg - 50mg	79 - 161
Zoloft®	50mg – 200mg	80 - 165
Paxil®	20mg – 50mg	89 - 187
Paxil CR®	25mg – 62.5mg	96 - 186
Prozac®	20mg – 80mg	92 - 445
	90mg¶/week	90

*Common dose ranges were obtained from the Drug Facts and Comparisons®, AHFS Drug Information®, and the Physicians' Desk Reference®.
†Average wholesale (AWP) and HCFA/MAC prices: Facts and Comparisons (Medi-Span), St Louis, MO; October 2003. Costs may vary depending on tablet strength combinations.
‡The pricing for fluoxetine and paroxetine were obtained from products that are rated by the FDA as meeting bioequivalence requirements (AB rating) to Prozac® and Paxil® respectively.
§ note that the HCFA or MAC (maximum allowable cost) pricing on generic fluoxetine is $ 0.60 per 20 mg capsule and $4.01 per 40 mg capsule. If appropriate for the patient, multiple units of 20mg fluoxetine could be utilized to obtain the desired dose at a lower cost (e.g., taking 2 x 20mg capsules per day would result in an AWP of $36 per month compared to $120.30 taking 1 x 40mg capsule)
¶Prozac® 90mg per week indicated for continuation treatment phase of major depressive disorder.

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Introducing Heritage Information Systems, Inc.:

By Craig Boon, MS, Director, Account Management and Margaret Cavanaugh, R.Ph., Pharmacotherapy Specialist

Heritage Information Systems, Inc. (Heritage) was selected to provide Clinical Management Services for the Kansas Medical Assistance Program. Heritage, a privately held company, currently provides services to some of the largest payers of prescription drug benefits in the country, including thirteen state Medicaid agencies. Heritage has four office locations—a main office in Richmond, Virginia and satellite offices in Miami, Florida, Oahu, Hawaii, and Jefferson City, Missouri—as well as permanent staff in Pennsylvania and Michigan to serve its clients. Heritage's two divisions, Cost Containment and Clinical Management Services, were developed to help clients improve quality of care for patients while minimizing costs. The Cost Containment division specializes in healthcare auditing for all aspects of the pharmacy benefit.

The Clinical Management division specializes in prior authorization and prospective drug utilization review (ProDUR) editing programs, retrospective drug usage evaluation (DUE), development and implementation of disease management programs, pharmacoeconomic and outcomes analyses, and pharmacy program consulting services. Recently, Heritage performed an assessment of KMAP's prescription drug program to identify potential areas for improvement. During the period of July 2002 through June 2003, KMAP spent just over $232 million on a total of approximately 4.5 million prescriptions. The average amount paid per claim was $52.03. Heritage is currently working with KMAP to identify and act upon the primary issues affecting costs and the quality of care for Medicaid recipients.

The following table lists therapeutic classes ranked by amount paid for the Kansas Medical Assistance Program.

Therapeutic Class Ranking by Total Dollars Paid
July 2002 – June 2003

Therapeutic Class	Paid*	Number of Prescriptions
CNS Agents	$110,978,371	1,596,157
Cardiovascular Agents	$22,808,635	751,307
Miscellaneous Agents†	$22,772,254	517,522
GI Agents	$18,668,276	277,728
Respiratory Agents	$16,993,365	376,784
Anti-infective Agents	$15,765,072	391,165
Antidiabetic Agents	$9,008,292	172,856
Hormonal Agents	$8,178,621	281,510
Hematological Agents	$5,604,549	88,546
Antineoplastic Agents	$1,617,843	13,054
TOTAL	**$232,395,278**	**4,466,629**

***Reflects cost per ingredient plus dispensing fee and before manufacturer rebates**
† includes immunological/biological agents, electrolytes and minerals, genito-urinary agents, ear-eyes-nose-throat products and topical agents.